

WHAT IS CLAIMED IS:

1. An in vitro assay for modulators of a nuclear hormone receptor function, comprising steps:

forming a mixture comprising a first nuclear hormone receptor, a peptide sensor and a candidate agent, but not a natural coactivator protein of the first receptor, wherein the sensor provides direct, assay detectable binding to the first receptor under assay conditions

measuring an agent-biased binding of the sensor to the first receptor;

comparing the agent-biased binding with a corresponding unbiased binding of the sensor to the first receptor;

wherein a difference between the biased and unbiased bindings indicates that the agent modulates a function of the first receptor.

2. A method according to claim 1, wherein the first receptor comprises the ligand binding domain of PPAR $\gamma$ , Cyp7PBP(LRH-1), NURR1, RZR $\beta$ , ROR $\alpha$ , NOR-1, Rev-ErbA $\beta$ , Tlx, NGFI-B $\beta$ , HZF-2 $\alpha$ , COUP-TF $\alpha$ ,  $\beta$ ,  $\gamma$ , Nur77, LXR $\alpha$ , COR, Rev-ErbA $\alpha$ , HNF4 $\alpha$ , TOR, MB67 $\alpha$ , SHP, FXR, SF-1, LXR $\beta$ , GCNF, TR2-11 $\alpha$ ,  $\beta$ , TR4, ERR $\alpha$ ,  $\beta$  and DAX-1

3. A method according to claim 1, wherein the agent effects an increase in binding of the sensor to the first receptor.

4. A method according to claim 1, wherein the sensor is at a concentration of less than about 10 nM.

5. A method according to claim 1, wherein the sensor comprises an amphipathic alpha helix.

6. A method according to claim 1, wherein the sensor comprises the sequence L<sub>1</sub>X<sub>1</sub>X<sub>2</sub>L<sub>2</sub>L<sub>3</sub>, wherein L<sub>1</sub>-L<sub>3</sub> are independently selected from hydrophobic amino acids and X<sub>1</sub>-X<sub>2</sub> are independently selected from any amino acid.

7. A method according to claim 1, wherein the sensor comprises a peptide sequence selected from KLVQLLT<sub>TT</sub> (SEQ ID NO:1), ILHRLLQE (SEQ ID NO:2), LLRYLLDK

(SEQ ID NO:3), LLRYLLD (SEQ ID NO:4), LRYLLD (SEQ ID NO:5), LLRYLL (SEQ ID NO:6), LRYLL (SEQ ID NO:7), LLRYLLDKD (SEQ ID NO:8), QLLRYLLDKD (SEQ ID NO:9), HQLLYLLDKD (SEQ ID NO:10), PQAQQKSLQQLLT (SEQ ID NO:11), LLQQLLTE (SEQ ID NO:12), VTLLQLLG (SEQ ID NO:13), ILRKLLQE (SEQ ID NO:14), ILKRLLE (SEQ ID NO:15), ILRRLLE (SEQ ID NO:16) and ILKKLLQE (SEQ ID NO:17).

8. A method according to claim 1, wherein the first receptor, peptide and agent are in solution.

9. A method according to claim 1, wherein the peptide comprises a fluorescent label and the measuring step comprises detecting fluorescence polarization of the label.

10. A method according to claim 1, wherein the mixture further comprises a ligand of the first receptor.

11. A method according to claim 1, wherein the sensor provides direct, assay detectable, ligand dependent binding to the first receptor under assay conditions.

12. A mixture consisting essentially of a nuclear hormone receptor, a candidate agent and a peptide comprising the sequence  $L_1X_1X_2L_2L_3$  covalently coupled to a detectable label, wherein  $L_1-L_3$  are independently selected from hydrophobic amino acids and  $X_1-X_2$  are independently selected from any amino acid and wherein the peptide provides direct, in vitro ligand-dependent binding to the receptor.

13. The mixture of claim 12, in which the binding is enhanced in the presence of the agent.

14. A mixture consisting essentially of a nuclear hormone receptor, a ligand of the receptor, a candidate agent, and a peptide comprising the sequence  $L_1X_1X_2L_2L_3$  covalently coupled to a detectable label, wherein  $L_1-L_3$  are independently selected from hydrophobic

amino acids and  $X_1$ - $X_2$  are independently selected from any amino acid and wherein the peptide provides direct, in vitro ligand-dependent binding to a nuclear hormone receptor.

5 15. A sensor consisting essentially of a peptide comprising the sequence  $L_1X_1X_2L_2L_3$  covalently coupled to a detectable label, wherein  $L_1$ - $L_3$  are independently selected from hydrophobic amino acids and  $X_1$ - $X_2$  are independently selected from any amino acid and wherein the peptide provides direct, in vitro ligand-dependent binding to a nuclear hormone receptor.

10 16. A sensor according to claim 15, wherein the label is a fluorescent label coupled to the N-terminus of the peptide and the peptide is 12 or fewer residues in length.

15 17. A method according to claim 1, wherein the measuring step comprises detecting the sensor of immobilized first receptor-sensor complexes.

18. A method according to claim 1, wherein the measuring step comprises detecting the receptor of immobilized first receptor-sensor complexes.

20 19. A method according to claim 1, wherein the measuring step, the first receptor is immobilized through the sensor.

20. A method according to claim 1, wherein the sensor comprises a label and wherein the measuring step, the first receptor is immobilized through the sensor and the sensor is immobilized through the label.

25 21. A method according to claim 1, wherein the sensor comprises a label and wherein the measuring step, the first receptor is immobilized through the sensor, and the sensor is immobilized through the label by a second receptor.

30 22. A method according to claim 1, wherein the sensor comprises a label and wherein the measuring step, the first receptor is immobilized through the sensor, and the sensor is immobilized through the label by a second receptor and wherein the measuring step

comprises detecting the immobilized first receptor.

23. A method according to claim 1, wherein the sensor comprises a label and wherein the measuring step, the first receptor is immobilized through the sensor, and the sensor is immobilized through the label by a second receptor and wherein the measuring step  
5 comprises detecting the immobilized first receptor with a third receptor.

24. A method according to claim 1, wherein the sensor comprises an epitope label, wherein the measuring step, the first receptor is immobilized through the sensor and the sensor is immobilized through the label by a second receptor comprising an immobilized  
10 epitope label-specific antibody moiety.

25. A method according to claim 1, wherein the sensor comprises a biotin label and wherein the measuring step, the first receptor is immobilized through the sensor and the sensor is immobilized through the label by a second receptor comprising an immobilized  
15 avidin moiety.

26. A method according to claim 1, wherein the measuring step, the sensor is immobilized through the first receptor.

27. A method according to claim 1, wherein the measuring step, the sensor is immobilized through the first receptor and the first receptor is immobilized through a second receptor.  
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28. A method according to claim 1, wherein the measuring step, the sensor is immobilized through the first receptor and the first receptor is immobilized through a second receptor and  
25 wherein the measuring step comprises detecting the immobilized sensor.

29. A method according to claim 1, wherein the measuring step, the sensor is immobilized through the first receptor and the first receptor is immobilized through a second receptor and wherein the measuring step comprises detecting the immobilized sensor with a third receptor.  
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30. A method according to claim 1, wherein the measuring step, the sensor is immobilized

add C57

Good!